UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,321	11/22/2006	Axel Kallies	20155	6068

23389 7590 04/01/2009

SCULLY SCOTT MURPHY & PRESSER, PC
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
04/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,321	KALLIES ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-5,8-34 and 37-47* is/are pending in the application.

4a) Of the above claim(s) *28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8-27,30-34 and 37-47* is/are rejected.

7)☒ Claim(s) *37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 6, 7, 35, and 36 have been cancelled. Claims 28 and 29 have been withdrawn. Claims 1-5, 17-20, 22, 30, 31, 33, 34, 37, 44, and 45 have been amended.

Claims 1-5, 8-27, 30-34, and 37-47 are under examination.

Specification

2. The disclosure remains objected to for the reasons of record set forth in the non-final Office action of 09/15/2008.

Applicant submits that the specification has been amended to delete the term "functional" on p. 66 and to delete the symbol appearing on p. 71. However, the Examiner was unable to find such amendments. For this reason, the objection is maintained.

3. All rejections pertaining to claims 6, 7, 35, and 36 are moot because Applicant cancelled the claims in the reply filed on 01/13/2009.

The objections to claims 17-19, 26, 27, and 30 for containing minor informalities are withdrawn in response to Applicant's amendments to the claims filed on 01/13/2009.

The rejection of claim 37 under 35 U.S.C. 112, second paragraph, as being lacking antecedent basis for the limitation "genetic material" in claim 31 is withdrawn in response to Applicant's amendments to the claims filed on 01/13/2009.

The rejection of claims 1-5, 8-27, 30-34, and 37-47 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in response to Applicant's amendments to the claims filed on 01/13/2009.

The rejection of claims 1, 2, 8, 10, 11, 17, 19-25, 31, 44, 45, and 47 under 35 U.S.C. 102(b) as being anticipated by Chang et al. (Nat. Immunol., 2000, 1: 169-176) is withdrawn in response to Applicant's amendments to the claims filed on 01/13/2009.

The rejection of claims 1-5, 8-27, 30-34, and 37-47 under 35 U.S.C. 103(a) as being unpatentable over Glimcher et al. (PGPUB 2002/0059652), in view of both Shaffer et al. (Immunity, 2002, 17: 51-62) and Mountford et al. (Proc. Natl. Acad. Sci. USA, 1994, 91: 4303-4307) is withdrawn in response to Applicant's amendments to the claims filed on 01/13/2009.

New Rejections/Objections

Claim Objections

4. Claim 37 is objected to because of the following informalities: the claim recites "wherein the cells, modified Blimp allele or the reporter gene is derived". Appropriate correction to "wherein the cells, modified Blimp allele or the reporter gene are derived" is required.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-5, 8-27, 30-34, and 37-47 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Glimcher et al. (PGPUB 2002/0059652. of record), in view of each Shaffer et al. (Immunity, 2002, 17: 51-62, of record), Pol et al. (Journal of Biomolecular Screening, 2002, 7: 325-332), and Mountford et al. (Proc. Natl. Acad. Sci. USA, 1994, 91: 4303-4307, of record).

Glimcher et al. teach a method of *in vitro* or *in vivo* screening for agonists or antagonists of terminal differentiation of B- or T-cells, the method comprising contacting a test compound with B- or T-cells, wherein the B- or T-cells are ASC or $CD4^+$cells and could be of mouse origin, and wherein the test compound modulates the activity of XBP-1 transcription factor in the B- or T-cells (claims 1, 8-16, 30, 37, 38-43) (Abstract; p. 1, paragraphs 0004 and 0006; p. 2, paragraph 0008; p. 3, paragraphs 0019 and 0021; p. 4, paragraph 0031; p. 5, paragraphs 0042 and 0053; p. 11, paragraph 0097).

Glimcher et al. do not teach screening for compounds capable of modulating Blimp-1 activity (claims 1 and 30). However, they do teach that the XBP-1 transcription factor acts downstream of Blimp-1 (p. 24-25, paragraphs 0214 and 0215). Additionally, Shaffer et al. teach that Blimp-1 is the master regulator of plasma cells terminal differentiation, wherein Blimp acts by allowing the expression of specific transcription factors such as XBP-1 (Abstract, p. 56, Fig. 3, p. 59, Fig. 7, p. 60, column 1, last

paragraph, column 2). Based on these teachings, it would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Glimcher et al. by substituting their XBP-1 with Blimp-1 to achieve the predictable result of screening for agonists or antagonists of terminal differentiation of B- or T-cells.

Glimcher et al. and Shaffer et al. do not teach inserting a nucleic acid encoding a reporter molecule into an intron of the *blimp* locus to obtain a modified *blimp* allele comprising the Blimp coding sequences and the reporter under the control of the endogenous *blimp* regulatory elements (claims 1-3 and 30-32). However, doing such was suggested by the prior art. For example, Pol et al. teach that high-throughput screening methods require readouts other than determining the level or activity of the gene of interest. Pol et al. suggest using homologous recombination to place a reporter such as GFP under the control of the endogenous regulatory elements of the gene of interest, wherein the detection of the reporter indicates a cellular phenotype (claims 17 and 19) (Abstract; p. 325, column 1; p. 326, column 1; p. 327, column 2, third and fourth full paragraphs; p. 331, paragraph spanning columns 1 and 2). It is noted that, at the time the invention was made, homologous recombination to obtain cells comprising homozygous or heterozygous modifications was routine in the prior art. For example, Mountford et al. teach using homologous recombination in ES cells to place reporters under the control of regulatory sequences of endogenous genes of interest with or without modifying the endogenous gene, wherein insertion could be within an exon or within an intron (claims 3, 18, and 32) (Abstract, p. 4303, column 2 and Fig. 1). Based on these teachings, it would have been obvious to one of skill in the art, at the time the

invention was made, to modify the method of Glimcher et al. and Shaffer et al. by using homologous recombination to place GFP into an intron of the *blimp* allele to achieve the predictable result of obtaining a genetically modified cell suitable for high-throughput screening of test agents capable of modulating Blimp-1 activity. It is noted that by going so, one of skill in the art would have used a targeting vector as recited in claims 44-47. Additionally, by practicing the screening method according to the combined teachings of Glimcher et al., Shaffer et al., Pol et al., and Mountford et al., one of skill in the art would also have practiced a method of monitoring a B or T-cell, wherein detection of the reporter indicates the commitment of the B or T-cell to terminally differentiate (claims 20-27).

Applicant's arguments are answered below to the extent that they pertain to the instant rejection.

Applicant traversed the instant rejection on the grounds that the problem to be solved by the present invention is how to detect terminal differentiation of haematopoietic cells; the solution is provided by the targeted insertion of a reporter sequence into the endogenous Blimp gene sequence. In contrast, Applicant argues, the problem to be solved by Glimcher et al. is how to regulate hepatocyte growth, plasma cell differentiation and T-cell subset activity. Applicant argues that Glimcher et al. identify agents which modulate XBP-1 by assessing a change in XBP-1 expression; there is no recognition by Glimcher et al. that terminal differentiation of haematopoietic cells is linked to Blimp. Accordingly, Applicant argues, those skilled in the art would not

have even been motivated to look to Glimcher et al. for a solution to the problem of detecting terminal differentiation of haematopoietic cells.

Applicant's arguments are acknowledged, however they are not found persuasive because Glimcher et al. do teach that the XBP-1 transcription factor acts downstream of Blimp-1, i.e., Glimcher et al. recognize that the terminal differentiation of haematopoietic cells is linked to Blimp (see above). Furthermore, the prior art teaches Blimp-1 as the master regulator of plasma cells terminal differentiation, wherein Blimp acts by allowing the expression of specific transcription factors such as XBP-1 (see the teachings of Shaffer et al. above). Therefore, one of skill in the art would have known to that substituting XBP-1 with Blimp-1 would achieve the same result. For these reasons, the rejection is maintained.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Examiner, Art Unit 1633